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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/608,918	06/30/2000	Scott R. Presnell	99-50	2697

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EXAMINER
PRASAD, SARADA C

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/608,918	PRESNELL ET AL.	
	Examiner	Art Unit	
	Sarada C Prasad	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-16 and 18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: Seq. alignment

Detailed Action

1. Applicant's election of Group I drawn to SEQ ID No. 2 in Paper No. 9 (3/18/02) is acknowledged. Applicants request to combine Groups I & II (claims 1-7, 17), Groups III & IV, Groups V & VI, Groups VII & VIII, Groups IX & X, and Groups XI & XII into a single category, and examine together because they are both classified in class 530 subclass 350 and evaluation in one search, and assert that it would not pose undue burden to the Examiner (page 3 last para of response in Paper No. 9). This argument has been found to be partly persuasive and Groups I and II have been combined. Currently claims 1-7, and 17 with respect to SEQ ID No. 2 and SEQ ID No. 10 are under consideration for examination, and claims 8-16, and 17-20 are withdrawn from consideration as being non-elected.

Specification

2a. Title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

2b. Claim 3 is objected to due to recitation of 'SEQ ID No. 11 and SEQ ID No. 12 ' which are directed to non-elected invention. This objection would be obviated by recitation of only elected SEQ ID Nos.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-7, and 17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial asserted utility or a well-established utility.

The instant application has provided a description of a polypeptide termed Zcytor14, which exhibits extremely high homology to IL-17 receptor (see attached sequence alignment A). In particular, polypeptide of SEQ ID No. 2 representing the full length 692 amino acid protein, and the mature polypeptide of SEQ ID NO. 10 of 688 residues have been disclosed (pages 2-4 of specification). The breadth of biological functions and possible uses disclosed in the specification are largely dependent upon the structural homology of the instant Zcytor14 polypeptide to IL-17 receptor (page 70 of specification, 3rd para, lines 1-2). The specification also asserts that since IL-17 plays a pivotal role in initiating or sustaining an inflammatory response, IL-17 activates the production of inflammatory mediators by synoviocytes, and that IL-17 contributes to the proinflammatory pattern that is characteristic of rheumatoid arthritis, the instant Zcytor14 that has high degree of homology to IL-17 receptor can be used to treat inflammation, and conditions, such as rheumatoid arthritis that are associated with inflammation (page 70 of specification, 3rd para, lines 2-end).

The instant invention lacks patentable utility because the claimed effectiveness and functionality of the Zcytor14 are hypothetical. It is clear from the instant specification that the protein Zcytor14 of SEQ ID No. 2 is a homologue of IL-17 receptor and it has been assigned a functionality based on homology. There is little doubt that, after further characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claim of therapeutic utility as a novel cytokine is incomplete. Zcytor14 polypeptides have not yet been shown to have their own identity by way of demonstrated biological effects or functions. In the instant case the homology between instant SEQ ID No. 2 and IL-17 receptor is as high as 99.5%.

However, it is possible that variants of a given polypeptide could have different functions. For example, Yan et al. disclose that ectodysplatin, a member of the TNF family, encoded by the EDA gene is represented by 2 members: EDA-A1 and EDA-A2 are two isoforms of ectosdysplatin that differ only by an insertion of two amino acids. This insertion functions to determine receptor-binding specificity, such that EDA-A1 binds only the receptor EDAR, where as EDA-A2 binds only the related, but distinct, X-linked ectodyspaltin-A2 receptor (XEDAR). *In situ* binding and organ culture studies indicate that EDA-A1 and EDA-A2 are differentially expressed and play a role in epidermal morphogenesis (entire abstract). Therefore, assignment of function based on homology alone is not necessarily realized when the proposed function has in fact not been realized. Instant specification contemplates proposed uses rather than disclose a specific, substantial use for the claimed polypeptides (pages 70-75 of specification).

The specification discloses expression of Zcytor14 gene in thyroid, adrenal gland, prostrate, and liver tissues, and less expression in heart, small intestine, stomach and tracheal tissues and no expression brain, placenta, lung, skeletal muscle, kidney, pancreas, spleen, thymus, testis, ovary, colon, peripheral blood leukocytes, spinal cord, lymph node and bone marrow (page of specification, last 4 lines). Such expression in different tissues is a general property shared by many proteins, and does not depend on any specific aspect of the observed expression pattern nor does such information lead to any practical application specific to the instant Zcytor14. Therefore, tissue specific expression patterns as disclosed would not constitute a specific or substantial use. Additionally, the activities of Zcytor14 and the claimed variants of 70%, 85% or 90% identity are assumed to be IL-17 receptor-like without disclosing the expected activity for even SEQ ID No. 2 or SEQ ID NO. 10. Therefore, in the absence of knowledge of

the biological significance of these proteins, there are no immediately obvious patentable uses for these receptors. Since the instant invention does not disclose a "real world" use for proteins of SEQ ID No. 2, the claimed invention is incomplete, and therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claims 1-7, and 17 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if the applicants were to establish a specific and substantial utility for Zcytor14, the specification would only be enabling for Zcytor14 polypeptides of SEQ ID No. 2 and SEQ ID No. 10, amino acid sequences selected from the group of amino acid residues 21-452 of SEQ ID No. 2, amino acid residues 21-435 of SEQ ID No. 10, amino acid residues 21-677 of SEQ ID No. 2, amino acid residues 1-692 of SEQ ID No. 2, wherein the isolated polypeptide specifically binds with an antibody that specifically binds with a polypeptide consisting of either the amino acid sequence of SEQ ID No. 2 or the amino acid sequence of SEQ ID No. 10, but the specification is non enabling for variants of the polypeptides that have at least 70% or 80% or 90% identical to the reference amino acid sequence as recited in claims 1 and 2.

The factors considered when determining if the disclosure satisfies enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

What the specification sets forth:

The specification sets forth for SEQ ID No. 2 and SEQ ID No. 10 and portions of the polypeptides with functional limitations such as extracellular domain (21-452 of SEQ ID No. 2; 21-435 of SEQ ID No. 10) , transmembrane domain (453-473 of SEQ ID No. 2), intracellular domain (474-677 of SEQ ID No. 2 or 457-673 of SEQ ID No. 10), or a secretory sequence (1-20 of SEQ ID No. 2) (pages 2-4 of specification).

Instant rejection of these claims 1-2 under 35 USC 112 first paragraph is based on the fact that each of these claims are drawn to sequences comprising fragments of SEQ ID No. 2 or 10 with variable identities. One of skill in the art could not predictably make and use such sequences since requirements for a functional molecule are not disclosed. Applicants have not provided guidance in the form of properties or characteristics of the sequences that are required to represent a minimally functional extracellular region or other properties of the sequence essential to any function. Thus, the critical features or the essential characteristics of the polypeptides are not provided. Thus, a skilled artisan would require additional guidance, in ways to determine which of these polypeptide fragments would have the desired characteristics of the disclosed Zcytor14 sequence and could therefore be enabled for use. Ability of the polypeptides to bind to an antibody that binds to SEQ ID NO. 2 or SEQ ID No. 10 does not provide adequate criterion for a functional limitation because epitopic regions can be present in more than one protein, some of which may be unrelated to the polypeptide under consideration. Even if the antibody binds, it does not predict functional use of the polypeptide fragments nor sets forth critical features of the polypeptide fragments. For example, the specification also proposes to make chemically modified compositions, as well as fragments entirely based on antibody binding that might not be functionally equivalent. The instant specification fails to

provide sufficient guidance, such as definitive structural/functional features of the claimed genus of polypeptides so one of skill in the art could make them and use them.

Additionally, no guidance is provided for one of skill in the art as to the sites at which variability may be tolerated, or how fragments or portions having minimally 70% homology to the extracellular domain function relative to the full length sequence of 692/688 amino acids of either SEQ ID No. 2/SEQ ID No. 10. Furthermore, prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed by the instant claims. Predictability in the art suggests that change of even one or two amino acid residues can influence the expected activity of a given polypeptide as discussed above as part of the 35 USC 101-utility rejection (Yan et al. 2000).

Therefore, based on predictability in the art pointing to even a change in two amino acids could alter the function of a polypeptide, and lack of adequate guidance for making and use of claimed variants, it would require undue experimentation for one of skill in the art to practice the invention as claimed. Accordingly, even if activity were established, the specification is non-enabling for practice of full scope of claims 1, 2.

Written Description

4b. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification proposes certain distinct fragments of SEQ ID No. 2 and 10 that might possess a combination of critical structural features and functional correlation, for

example, the extracellular domain (21-452 of SEQ ID No. 2; 21-435 of SEQ ID No. 10) , transmembrane domain (453-473 of SEQ ID No. 2), intracellular domain (474-677 of SEQ ID No. 2 or 457-673 of SEQ ID No. 10), or a secretory sequence (1-20 of SEQ ID No. 2) (pages 2-4 of specification). However, the specification is non enabling for recitation of isolated polypeptides comprising amino acid sequences that are at least 70%, 80% or 90% identical to either full-length or portions of SEQ ID No. 2 or SEQ ID No.10 in the claim language, because claims 1 and 2 recite % identity language, without recitation of corresponding functional limitations of the variant polypeptides. Recitation of antibody binding as a functional limitation is not adequate because immunogenic epitopes need not necessarily be related to functional criteria, while they can also occur in proteins of unrelated function. Instant claims drawn to variant polypeptides of SEQ ID NO. 2 and 10 encompass a large genus of polypeptides without description as to what the critical features of those polypeptides are such that one could readily envisage the genus as claimed. The claims as written encompass polypeptides, which vary substantially in length and also in amino acid sequence. The instant disclosure of polypeptides of SEQ ID Nos.2 and 10 does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of sub genera including full-length polypeptides, variants and polypeptides functionally unrelated to the proposed Zcytor14 of the instant invention. There is no description of the conserved regions, which are critical to the structure, and function of the genus claimed. The specification proposes to discover other members of the genus by using techniques involving probes, primers, hybridization and antibodies. The applicant is asking for permission to perform further experimentation.

Based on the above discussion, one of skill would reasonably conclude that the disclosure fails to provide a representative number of species of the polypeptide variants of SEQ ID No. 2 and enable the genus as broadly claimed. Accordingly, the specification is non-enabling for practice of instant claims 1 and 2.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

WO200146420-A2 (28-JUN-2001) discloses a protein sequence identified as human IL-17 receptor that is 99.5% identical to instant SEQ ID No. 10.

Conclusion

5a. SEQ ID No. 2 and 10 are free of prior art.

5b. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday - Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.
Examiner
Art Unit 1646
May 27th, 2002.

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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